

AMENDMENTS TO THE CLAIMSClaim Listing

1-69 (canceled)

70. (Currently Amended) An isolated monoclonal antibody or a fragment thereof that binds at least two different human inhibitory KIR receptor gene products, wherein said antibody or fragment thereof is capable of neutralizing KIR-mediated inhibition of natural killer (NK) cell cytotoxicity in NK cells expressing at least one of said two different human inhibitory KIR receptors, wherein said monoclonal antibody or fragment thereof is:

- a) the DF200 antibody produced by the hybridoma DF200, deposited as CNCM I-3224;
- b) a chimeric antibody comprising the variable region binding domains of the DF200 antibody;
- c) a humanized antibody comprising the CDRs of the DF200 antibody; or
- d) an Fab_a or $F(ab')_2$ ~~fragment~~ Fab' , Fab' -SH, $F(ab')_2$, or Fv fragment of any one of the antibodies set forth in a), b) or c).

71. (Previously Presented) The isolated monoclonal antibody or a fragment thereof according to claim 70, wherein said antibody is the DF200 antibody produced by the hybridoma DF200, deposited as CNCM I-3224.

72. (Currently Amended) The isolated monoclonal antibody or a fragment thereof according to claim 70, wherein said fragment is an Fab_a or $F(ab')_2$ Fab' , Fab' -SH, $F(ab')_2$, or Fv fragment of the DF200 antibody.

73. (Previously Presented) The isolated monoclonal antibody or a fragment thereof according to claim 70, wherein said antibody is a chimeric antibody comprising the variable

region binding domains of the DF200 antibody.

74. (Currently Amended) The isolated monoclonal antibody or a fragment thereof according to claim 70, wherein said fragment is an ~~Fab₂~~ F(ab')₂, Fab', Fab'-SH, F(ab')₂, or Fv fragment of said chimeric antibody.

75. (Previously Presented) The isolated monoclonal antibody or a fragment thereof according to claim 70, wherein said antibody is a humanized antibody comprising the CDRs of the DF200 antibody.

76. (Currently Amended) The isolated monoclonal antibody or a fragment thereof according to claim 70, wherein said fragment is an ~~Fab₂~~ F(ab')₂, Fab', Fab'-SH, F(ab')₂, or Fv fragment of said humanized antibody.

77. (Previously Presented) The isolated monoclonal antibody or fragment thereof according to claim 70, wherein said monoclonal antibody or fragment thereof binds to KIR2DL1 and KIR2DL2/3.

78. (Withdrawn) An isolated monoclonal antibody or fragment thereof according to claim 70 conjugated or covalently bound toxin, detectable moiety, or solid support.

79. (Currently Amended) A composition comprising a pharmaceutically acceptable excipient and a monoclonal antibody or a fragment thereof that binds at least two different human inhibitory KIR receptor gene products, wherein said antibody or fragment thereof is capable of neutralizing KIR-mediated inhibition of NK cell cytotoxicity in NK cells expressing at least one of said two different human inhibitory KIR receptors, wherein said monoclonal antibody or fragment thereof is:

- a) the DF200 antibody produced by the hybridoma DF200, deposited as CNCM I-3224;
- b) a chimeric antibody comprising the variable region binding domains of the DF200

antibody;

c) a humanized antibody comprising the CDRs of the DF200 antibody; or

d) an ~~Fab~~ F(ab')₂, Fab', Fab'-SH, F(ab')₂, or Fv fragment of any one of the antibodies set forth in a), b) or c).

80. (Canceled)

81. (Previously Presented) The composition according to claim 79, wherein said antibody is the DF200 antibody produced by the hybridoma DF200, deposited as CNCM I-3224.

82. (Canceled)

83. (Previously Presented) The composition according to claim 79, wherein said antibody is a chimeric antibody comprising the variable region binding domains of the DF200 antibody.

84. (Previously Presented) The composition according to claim 79, wherein said fragment is an Fab or F(ab')₂ fragment of said chimeric antibody.

85. (Previously Presented) The composition according to claim 79, wherein said antibody is a humanized antibody comprising the CDRs of the DF200 antibody.

86. (Previously Presented) The composition according to claim 79, wherein said fragment is an Fab or F(ab')₂ fragment of said humanized antibody.

87. (Previously Presented) The composition according to claim 79, wherein said monoclonal antibody or fragment thereof binds to KIR2DL1 and KIR2DL2/3.

88. (Currently Amended) An isolated human, humanized or chimeric monoclonal antibody or a fragment thereof that binds Killer Ig-Like Receptors (KIRs) KIR2DL1 and KIR2DL2/3, wherein said human, humanized or chimeric antibody or fragment thereof is capable of neutralizing or inhibiting KIR-mediated inhibition of NK cell cytotoxicity ~~in~~ by NK cells

expressing any of the following (i) at least one of said KIR2DL1, (ii) and KIR2DL2/3 or (iii) a combination of KIR2DL1 and KIR2DL2/3.

89. (Currently Amended) A composition comprising a pharmaceutically acceptable excipient and ~~an~~ human, humanized or chimeric antibody or fragment thereof according to claim 88.

90. (Currently Amended) An isolated human, humanized or chimeric monoclonal antibody or a fragment thereof that binds Killer Ig-Like Receptors (KIRs) KIR2DL1 and KIR2DL2/3, wherein said antibody or fragment thereof is capable of neutralizing or inhibiting KIR-mediated inhibition of NK cell cytotoxicity in NK cells expressing any of the following (i) KIR2DL1, (ii) KIR2DL2/3 or (iii) at least one of said a combination of KIR2DL1 and KIR2DL2/3, wherein said human, humanized or chimeric monoclonal antibody or fragment thereof competes for binding to said KIR2DL1 and ~~or~~ KIR2DL2/3 on the surface of an NK cell with antibody DF200 produced by the hybridoma deposited as CNCM I-3224.

91. (Currently Amended) A composition comprising a pharmaceutically acceptable excipient and ~~an~~ human, humanized or chimeric antibody or fragment thereof according to claim 90.

92. (New) The isolated human, humanized or chimeric monoclonal antibody or fragment thereof according to Claim 88, wherein said antibody inhibits binding of HLA-C molecules to KIR2DL1 and KIR2DL2/3.

93. (New) The isolated human, humanized or chimeric monoclonal antibody or fragment thereof according to Claim 90, wherein said antibody inhibits binding of HLA-C molecules to KIR2DL1 and KIR2DL2/3.

94. (New) The isolated human, humanized or chimeric monoclonal antibody or fragment thereof according to Claim 92, wherein said HLA-C molecules are selected from Cw1, Cw2, Cw3, Cw4, Cw5, Cw6, an HLA-C molecule having a lysine residue at position 80, Cw7,

Cw8, and an HLA-C molecule having an asparagine residue at position 80.

95. (New) The isolated human, humanized or chimeric monoclonal antibody or fragment thereof according to Claim 93, wherein said HLA-C molecules are selected from Cw1, Cw2, Cw3, Cw4, Cw5, Cw6, an HLA-C molecule having a lysine residue at position 80, Cw7, Cw8, and an HLA-C molecule having an asparagine residue at position 80.

96. (New) The isolated human, humanized or chimeric monoclonal antibody or a fragment thereof of claim 88, wherein said antibody inhibits KIR2D-mediated inhibition of NK cell cytotoxicity by at least 50%.

97. (New) The isolated human, humanized or chimeric monoclonal antibody or a fragment thereof of claim 90, wherein said antibody inhibits KIR2D-mediated inhibition of NK cell cytotoxicity by at least 50%.

98. (New) The isolated human, humanized or chimeric monoclonal antibody or a fragment thereof of claim 88, which promotes lysis of matched or HLA compatible target cells by NK cells expressing KIR2DL1, KIR2DL2/3 or a combination thereof, wherein the target cells are not effectively lysed in the absence of the monoclonal antibody or fragment thereof.

99. (New) The isolated human, humanized or chimeric monoclonal antibody or a fragment thereof of claim 90, which promotes lysis of matched or HLA compatible target cells by NK cells expressing KIR2DL1, KIR2DL2/3 or a combination thereof, wherein the target cells are not effectively lysed in the absence of the monoclonal antibody or fragment thereof.

100. (New) The isolated human, humanized or chimeric monoclonal antibody or a fragment thereof of claim 98, wherein the NK cells in the absence of the monoclonal antibody or fragment bind to at least one HLA-C molecule selected from Cw1, Cw2, Cw3, Cw4, Cw5, Cw6, an HLA-C molecule having a lysine residue at position 80, Cw7, Cw8, an HLA-C molecule having an asparagine residue at position 80 and said binding is inhibited by said monoclonal antibody or fragment.

101. (New) The isolated human, humanized or chimeric monoclonal antibody or a fragment thereof of claim 99, wherein the NK cells in the absence of the monoclonal antibody or fragment thereof bind to at least one HLA-C molecule selected from Cw1, Cw2, Cw3, Cw4, Cw5, Cw6, an HLA-C molecule having a lysine residue at position 80, Cw7, Cw8, an HLA-C molecule having an asparagine residue at position 80, and said binding is inhibited by said monoclonal antibody or fragment.

102. (New) The isolated human, humanized or chimeric monoclonal antibody or a fragment thereof of claim 100, wherein the NK cells in the absence of the monoclonal antibody or fragment bind to at least one HLA-C molecule selected from Cw1, Cw3, Cw7, Cw8, and an HLA-C molecule having an asparagine residue at position 80, and said binding is inhibited by said monoclonal antibody or fragment.

103. (New) The isolated human, humanized or chimeric monoclonal antibody or a fragment thereof of claim 101, wherein the NK cells in the absence of the monoclonal antibody or fragment bind to at least one HLA-C molecule selected from Cw1, Cw3, Cw7, Cw8, and an HLA-C molecule having an asparagine residue at position 80, and said binding is inhibited by said monoclonal antibody or fragment thereof.

104. (New) The isolated human, humanized or chimeric monoclonal antibody or a fragment thereof of claim 100, wherein the NK cells in the absence of the monoclonal antibody or fragment bind to at least one HLA-C molecule selected from Cw2, Cw4, Cw5, Cw6 and an HLA-C molecule having a lysine residue at position 80, and said binding is inhibited by said monoclonal antibody or fragment.

105. (New) The isolated human, humanized or chimeric monoclonal antibody or a fragment thereof of claim 101, wherein the NK cells in the absence of the monoclonal antibody or fragment bind to at least one HLA-C molecule selected from Cw2, Cw4, Cw5, Cw6 and an HLA-C molecule having a lysine residue at position 80, and said binding is inhibited by said monoclonal antibody or fragment.

106. (New) The isolated human, humanized or chimeric monoclonal antibody or a fragment thereof of claim 100, wherein the NK cells in the absence of the monoclonal antibody or fragment bind to at least one HLA-C molecule selected from Cw1, Cw3, Cw7, Cw8, and an HLA-C molecule having an asparagine residue at position 80, and said binding is inhibited by said monoclonal antibody or fragment, and said NK cells further bind to, in the absence of the monoclonal antibody or fragment, at least one HLA-C molecule selected from Cw2, Cw4, Cw5, Cw6 and an HLA-C molecule having a lysine residue at position 80, and said binding is inhibited by said monoclonal antibody or fragment.

107. (New) The isolated human, humanized or chimeric monoclonal antibody or a fragment thereof of claim 101, wherein the NK cells in the absence of the monoclonal antibody or fragment bind to at least one HLA-C molecule selected from Cw1, Cw3, Cw7, Cw8, and an HLA-C molecule having an asparagine residue at position 80, and said binding is inhibited by said monoclonal antibody or fragment, and said target cells further bind to, in the absence of the monoclonal antibody or fragment, at least one HLA-C molecule selected from Cw2, Cw4, Cw5, Cw6 and an HLA-C molecule having a lysine residue at position 80, and said binding is inhibited by said monoclonal antibody or fragment.

108. (New) The composition of claim 89, which further comprises human immune cells.

109. (New) The composition of claim 91, which further comprises human immune cells.

110. (New) The isolated human, humanized or chimeric monoclonal antibody of Claim 88 or 90 that lacks an Fc region.

111. (New) The isolated human, humanized or chimeric monoclonal antibody or a fragment of a human or humanized antibody that binds Killer Ig-Like Receptors (KIRs) KIR2DL1 and KIR2DL2/3 according to claim 88, wherein said antibody or fragment does not comprise the variable light chain polypeptide in SEQ ID NO: 2.

112. (New) The isolated human, humanized or chimeric monoclonal antibody or a fragment of a human or humanized antibody that binds Killer Ig-Like Receptors (KIRs) KIR2DL1 and KIR2DL2/3 according to claim 90, wherein said antibody or fragment does not comprise the variable light chain polypeptide in SEQ ID NO: 2.

113. (New) The isolated human, humanized or chimeric monoclonal antibody of Claim 88 or 90 that has an Fc region that mediates low effector function.

114. (New) The isolated human, humanized or chimeric monoclonal antibody of Claim 113 that has an Fc region of IgG4 isotype.